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Review

Autophagy in organelle homeostasis: Peroxisome turnover

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Abstract

When cells are confronted with an insufficient supply of nutrients in their extracellular fluid, they may begin to cannibalize some of their internal proteins as well as whole organelles for reuse in the synthesis of new components. This process is termed autophagy and it involves the formation of a double-membrane structure within the cell, which encloses the material to be degraded into a vesicle called an autophagosome. The autophagosome subsequently fuses with a lysosome/vacuole whose hydrolytic enzymes degrade the sequestered organelle. Degradation of peroxisomes is a specific type of autophagy, which occurs in a selective manner and has been mostly studied in yeast. Recently, it was reported that a similar selective process of autophagy occurs in mammalian cells with proliferated peroxisomes. Here we discuss characteristics of the autophagy of peroxisomes in mammalian cells and present a comprehensive model of their likely mechanism of degradation on the basis of known and common elements from other systems.

Keywords: Lysosome; Pexophagy; Protein transport; Vacuole; Yeast

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Contents

1. Characteristic of peroxisome homeostasis

1.1. Morphology and function of peroxisomes

Peroxisomes are organelles found in nearly all eukaryotic cells. These organelles are usually elliptically shaped and have a diameter between 0.25 and 1 μm. In some types of tissues peroxisomes are tubularly shaped and connected to each other in a peroxisomal network, e.g. in rat hepatocytes (Yamamoto and Fahimi, 1987). They are an intracellular compartment involved in hydrogen peroxide metabolism and contain at least one hydrogen peroxide-producing enzyme along with catalase that is needed to eliminate this toxic compound.

In mammals, functional peroxisomes are required for a wide range of metabolic pathways, such as β- and α-oxidation of fatty acids, catabolism of amino acids, polyamines, and purines, as well as the synthesis of plasmalogens and cholesterol. A defect in peroxisomal function or formation causes several severe defects in humans. This is well demonstrated by human genetic disorders such as Zellweger syndrome, neonatal adrenoleukodystrophy, and infantile Refsum disease, which are characterized by mental retardation, severe neurologic, hepatic and renal abnormalities, and an early death (Small et al., 1988).

1.2. Peroxisome turnover

The size, number and enzyme content of peroxisomes can be very much influenced by the environment of the cell. For example peroxisomes are most abundant in tissues with active lipid metabolism, such as liver. There may be thousands of peroxisomes per cell in the mouse liver when animals are fed for a week with clofibrates, e.g. phthalate ester (DEHP). After withdrawal of the proliferators in 2 weeks, the